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DOCUMENT-IDENTIFIER: US 5738855 A

TITLE: Synthesis of typhoid fever vaccine from a plant or fruit polysaccharide

US PATENT NO. (1):

5738855

Drawing Description Text (2):

FIG. 1 shows the structure of the repeating unit of the Vi, the pectin and the O-acetylated pectin. For Vi, C.sub.2 (R) is N-acetylated and C.sub.3 (R.sup.1) is O-acetylated; for pectin, C.sub.2 and C.sub.3 are hydroxylated; for OAcPec, C.sub.2 and C.sub.3 are O-acetylated, n=number of subunits.

Detailed Description Text (2):

The Vi molecule of Salmonella typhi has a simple structure which is a linear polysaccharide having repeating sugar subunits. The antigenicity and immunogenicity of Vi depends on its N- acetyl at C.sub.2 and O-acetyl at C.sub.3 on each galacturonate subunit [19,23]. As shown for Vi and other polysaccharides, removal of the O-acetyls removed most of the antigenicity and all of the immunogenicity of the Vi [23,26]. The precise role of N-acetyl is not known as selective removal of the N-acetyl on Vi has not been accomplished. The present invention mimics the simple structure of Vi by modification of plant, fruit or synthetic saccharides. The modified plant, fruit or synthetic saccharides resemble Vi in antigenic and immunogenic properties and as such they have the capacity to act as an effective vaccines against typhoid fever.

Detailed Description Text (11):

The Vi molecule has N-acetyl groups at position C.sub.2 and O-acetyl groups at position C.sub.3. If all of the C.sub.2 positions have acetyl groups and all the C.sub.3 positions on Vi contain acetyl groups, then by definition, the Vi molecule is theoretically 200% fully acetylated. In most preparations of Vi the percent acetylation varies. The C.sub.2 position is usually about 100% N-acetylated and the C.sub.3 position is from about 60-90% O-acetylated depending on normal variation in preparations of Vi. The modified pectin, D-galacturonan, oligogalacturonate and polygalacturonate of the present invention approximates the total percent acetylation of Vi.

Detailed Description Text (18):

1) the M.sub.1 of Vi (about 2.1 times 10³ kD) is higher than that of OAcPec (about 400 kD); 2) the N-acetyl at C.sub.2 in the Vi is replaced by an O-acetyl in OAcPec and; 3) OAcPec has <5% neutral sugars and Vi had a nondetectable amount. At 3.degree.-8.degree. C., the stability of OAcPec as measured by its O-acetyl content and molecular size, is similar to that of Vi. At higher temperatures, the molecular size of Vi is more stable

than the OAcPec probably due to the stabilizing effect of a hydrogen bond between the N-acetyl and the carboxyl of the adjacent residue [23]. Since vaccines will be stored at -3°C to -8°C , the stability characteristic of OAcPec and Vi can be considered as similar.